Supravalvular Aortic Stenosis, Mental Retardation and a Characteristic Facies

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THE association of supravalvular aortic stenosis, multiple peripheral pulmonary arterial stenoses, mental and physical retardation and a characteristic facies is now well recognized as a syndrome.[1-4] This syndrome is of interest not only because of the difficulty of explaining its component parts in terms of a single pathological process, but also because it offers the astute clinician a chance of diagnosing a rare form of heart disease at a single glance of a patient. Furthermore, the remarkable similarity of the facies in patients with this syndrome to that found in children with infantile hypercalcemia of the severe type[5-7] suggests a possible etiology.

K.D., an 8-year-old boy, was admitted to Kingston General Hospital in 1960. He came from a family of 10 children. K.D. was the fourth-born child; all his siblings were alive and well except for a 3-year-old brother who had become mentally retarded following a febrile convulsive illness at the age of 2 years. Two other brothers were examined personally and found to be normal.

The mother was well during her pregnancy; she took no vitamin supplements. The baby was born at full term. The birth weight was 5½ lb., and the mother remarked that at birth he looked like "a little old man". When K.D. was 1 month of age, the mother was told that the child had a heart murmur. In the following months there were considerable feeding difficulties with episodes of vomiting which were treated by various changes of formula. The child was given a vitamin mixture (Poly-vi-sol) but only in the doses suggested by the prescribing doctors. Family photographs taken at 1 year of age show the typical "elfin" facies found in patients with infantile hypercalcemia[5] (Fig. 1). The child was slow in all aspects of his development; he sat up at the age of 18 months, crawled at 2 years of age, stood alone at 3½ years and walked alone at 4 years, at which age he was beginning to talk in sentences. There was no history of breathlessness or any reduction in his exercise tolerance.

Examination at the age of 8 years showed a child with a happy, carefree personality but obvious mental retardation. His height was 47 in. and weight 43 lb.; both measurements are below the third percentile for a boy of his age. He had a distinctive facies with a depressed nasal bridge and coarse pouting lips (Fig. 2). There was no strabismus. Examination of the heart showed a systolic thrill all over the precordium, maximum to the right of the sternum in the first intercostal space. There was a loud ejection murmur (grade 5 out of 6), widely heard over the precordium, maximal in the aortic area but transmitted through to the back

Fig. 1.—Patient at 1 year of age.

of the chest and even audible at the elbow. The second sound was single. The femoral pulses were palpable, the blood pressure was 115/80 mm. Hg, and there were no signs of cardiac failure. A diagnosis of aortic stenosis was made.

Cardiac catheterization, right and left, was carried

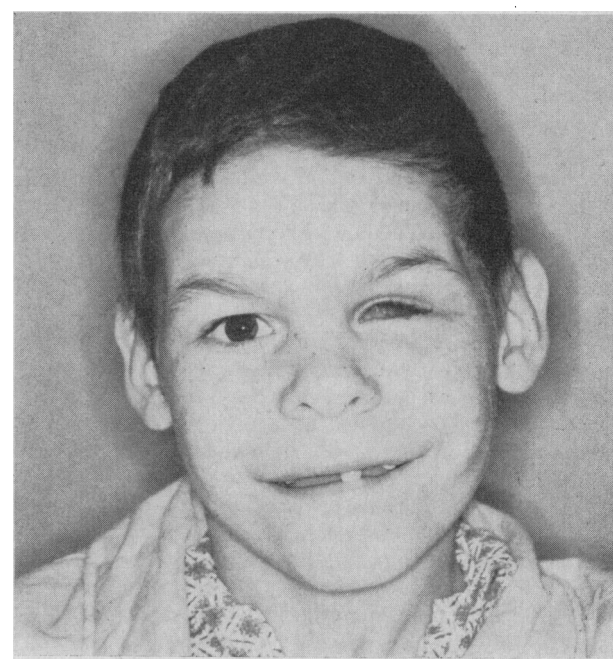

Fig. 2.—Patient at 12 years of age.

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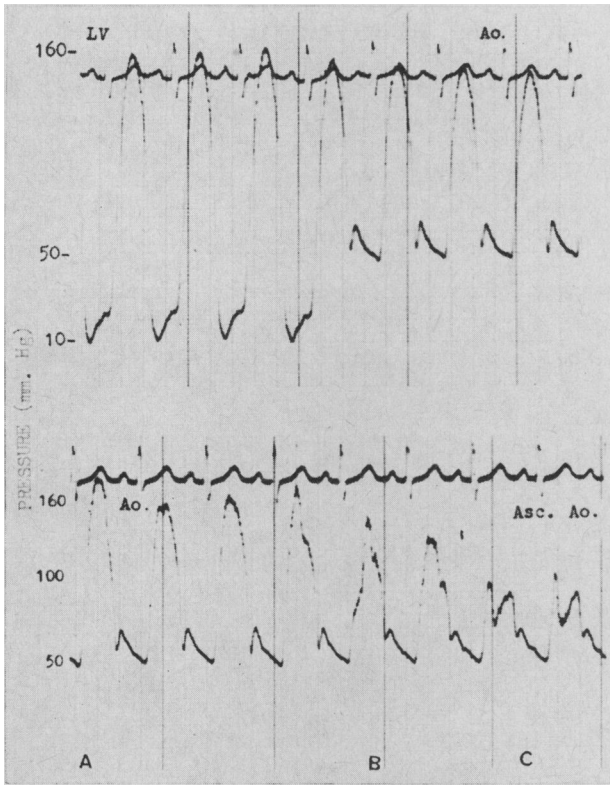

Fig. 3.—Tracing of left ventricular and aortic pressure curves obtained on withdrawing the catheter from the body of the left ventricle into the ascending aorta. This shows no pressure gradient across the aortic valve but reveals a pressure drop at B and a further fall-off in pressure at C, corresponding to the sites of supravalvular aortic constriction.

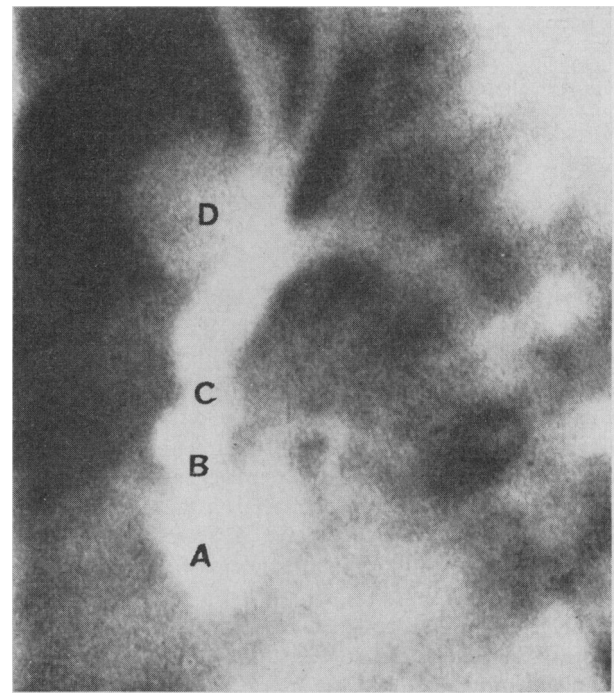

Fig. 4.—Aortogram showing the following features: A—Immediately above the valve there was no fall in the peak of the systolic pressure curve in this region, compared with the peak of the left ventricular pressure tracing. Constrictions are evident at B and C in the ascending aorta. The pressure curves above these points showed a fall in pressure, compared with the tracing obtained at A. Saccular widening of the aorta is illustrated at D.

out and showed a pressure of 85/0-8 mm. Hg in the right ventricle. The pressures in the right and left pulmonary arteries were 64/32 and 68/22, respectively. Left ventricular pressure was 170/20 and brachial artery pressure 105/55, confirming the clinical diagnosis of aortic stenosis. There was no evidence of shunting from the oxygen saturations.

At that time he was found to have a positive tuberculin reaction; a chest radiograph and gastric lavage for tubercle bacilli were negative. He was given a year's course of isoniazid.

The patient was followed up at regular intervals and in March, 1963, was readmitted to hospital because of an injury to the left eye. He developed panophthalmitis; and the eye was enucleated. Physical findings with respect to the heart had not altered in the intervening years. A repeat catheter study was carried out in May, 1963, and this showed a right ventricular pressure of 60/0-5 and a pulmonary artery pressure of 60/20. Transseptal puncture showed a left atrial pressure of 17/10. A Sones catheter was passed into the left ventricle and the left ventricular pressure was recorded as 160/10-22. Immediately above the aortic valve the pressure was 160/53. In the ascending aorta the pressure dropped to 95/51 (Fig. 3). Angiocardiography, with injection of dye into the left ventricle, demonstrated mitral regurgitation and showed that the aortic stenosis was in fact supravalvular (Fig. 4).

The boy was further investigated in November, 1964. There were no changes in the physical signs in the heart or cardiovascular system. It was noted that the retinal vessels in the right eye were excessively tortuous (Fig. 5). Slit-lamp examination of the cornea showed no opacities. Carotid arteriography showed similar tortuosity of the vessels of the brain (Fig. 6). Pulmonary artery angiography showed numerous peripheral pulmonary arterial stenosis with areas of poststenotic dilatation (Fig. 7).

The results of other investigations were as follows. At the age of 8 years I.Q. (W.I.S.C.) was 48; VDRL, negative. At the age of 11 years *Treponema pallidum* immobilization (TPI) tests were negative; serum proteins and electrophoretic pattern, normal; serum protein-bound iodine, 7.1 μg./100 ml.; and blood group, O, Rh positive. At the age of 12 years the serum calcium value was 10.3 mg./100 ml. and serum phosphorus, 5.5 mg./100 ml.; there was normal concentration and dilution of the urine; creatinine clearance was normal. Radiographs of the base of the skull and

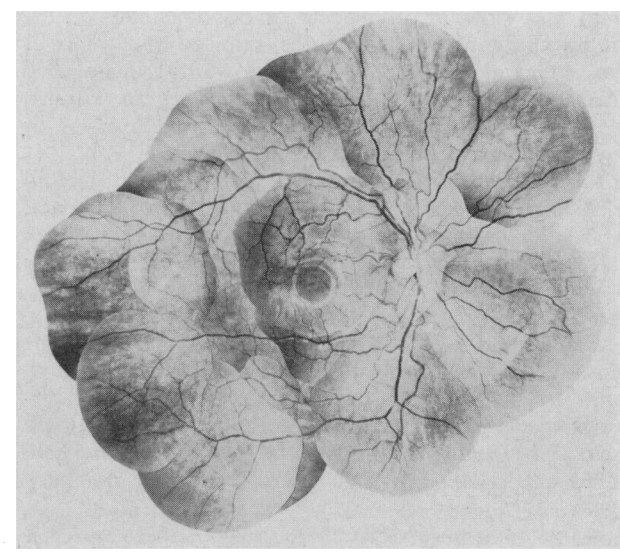

Fig. 5.—Retinal photograph showing tortuosity of vessels.

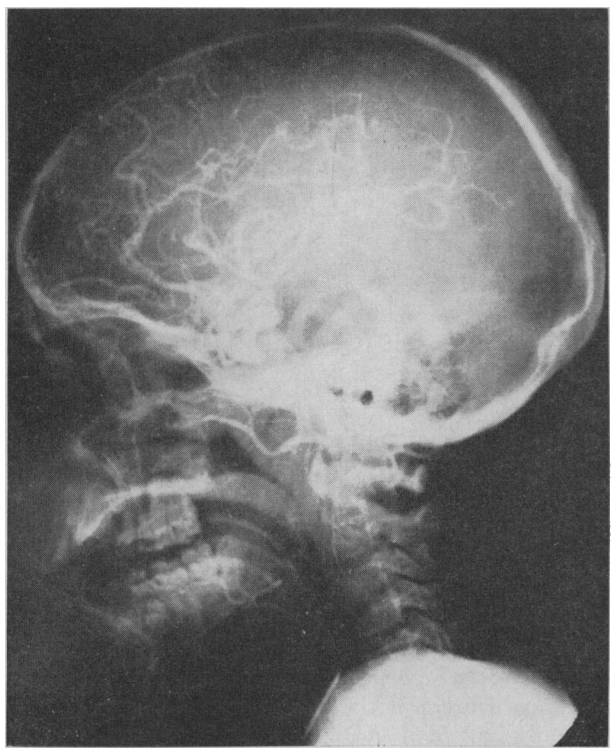

Fig. 6.—Cerebral angiogram. The arteries show marked tortuosity.

long bones showed no increased calcification. Buccal smear showed chromatin-negative cells, and examination of the chromosomes in the peripheral leukocytes revealed a normal karotype.

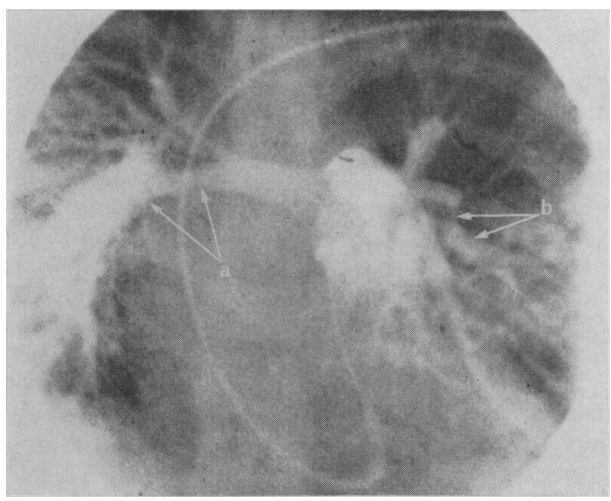

Fig. 7.—Areas of stenosis in the right and left pulmonary arteries with poststenotic dilatation (a & b).

DISCUSSION

This child's supravalvular aortic stenosis, the physical and mental retardation and the facies all fit into the syndrome described by Williams, Barratt-Boyes and Lowe.[1] In addition, the child had multiple peripheral pulmonary arterial stenoses, excessive tortuosity of the retinal vessels[7] and a carefree personality,[4, 7] all of which have been described in other patients with this syndrome. Although the failure to thrive and feeding difficulties in the early months of life, together with an "elfin" appearance, could have been due to infantile hypercalcemia,[5] we have no evidence that this was indeed the case. There was no history of excessive intake of vitamins either by the mother when she was pregnant or by the child, and no evidence of hypercalcemia at the age of 12 years, such as increased bone density, corneal opacities or reduced renal function. Furthermore, the child's systolic murmur was recognized at or before the age of 1 month, which supports the conclusion of Garcia *et al.*[6] that most, if not all, of the patients with this condition so far described had the aortic lesion from birth. If this is true, it is very difficult to attribute the peripheral arterial lesions to hypercalcemia unless this was present before birth. It seems more likely that hypercalcemia, when it occurs, is only one aspect of a more generalized disorder. Williamson[7] has suggested that there is a generalized vascular or connective tissue disorder in this syndrome and has speculated that a similar disorder might underlie the syndrome of idiopathic hypercalcemia of the severe type. Williams, Barratt-Boyes and Lowe[1] and Perou[8] had noted some clinical features in their patients suggestive of Marfan's syndrome. Chromosomal studies in several patients,[2] as well as our own, have so far shown no abnormality. Wooley *et al.*[9] and Eisenberg *et al.*[10] have described cases in which other members of the family were affected with the same aortic lesion. There was no suggestion of other affected children in the present family.

Clinically, the signs of a supravalvular aortic lesion cannot be distinguished from those of aortic stenosis. The best way to demonstrate the lesion is by injection of dye into the left ventricle and visualization of the aortic root and arch. Successful surgical correction of supravalvular aortic stenosis has now been carried out in a number of patients.[11, 12]

SUMMARY

A case of supravalvular aortic stenosis in a mentally retarded boy is described. The accompanying photographs show the characteristic facies in this rare syndrome. The relationship of this condition to infantile hypercalcemia is briefly discussed.

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